

A Targeted Review of Cost-Effectiveness of Immunotherapies Used in Treatment of Metastatic Non-Small-Cell Lung Cancer Patients in EU-5, Sweden, and Switzerland

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Background

- Lung cancer is the leading cause of cancer deaths worldwide, with an estimated 2.2 million new cases and 1.8 million deaths in 2020.¹
- Similar trends have been observed in Europe (EU) where 477,534 new cases were diagnosed, with a 5-year age-standardised prevalence of 77.8 per 100,000 in 2020.²
- Non-small cell lung cancer (NSCLC) accounts for 85% of all primary lung malignancies worldwide³ of which 70% are advanced (a) or metastatic (m)⁴, with 5-year survival rates of 6.0-7.0% across EU.^{5,6}
- Prognosis of mNSCLC (without driver mutations) remain poor with median overall survival (OS) of less than one year with standard of care (SoC) chemotherapy options.⁷
- Immune checkpoint inhibitors (ICIs) have shown an increase in median OS to 1 to 2 years in numerous clinical studies in patients with mNSCLC⁷⁻⁹, resulting in a paradigm shift in treatment of mNSCLC patients.
- Despite improved clinical outcomes, high cost of ICIs requires the evaluation of economic impact of these drugs.
- Hence, cost effectiveness analyses for various ICIs such as pembrolizumab, durvalumab, nivolumab, and atezolizumab were evaluated and summarised in this targeted review.

Objective

- To analyse published cost-effectiveness (CE) studies to understand the importance of ICIs and their role in decision making in mNSCLC in EU-5 (France, Germany, Italy, Spain, United Kingdom [UK]), Sweden and Switzerland, through a targeted literature review.

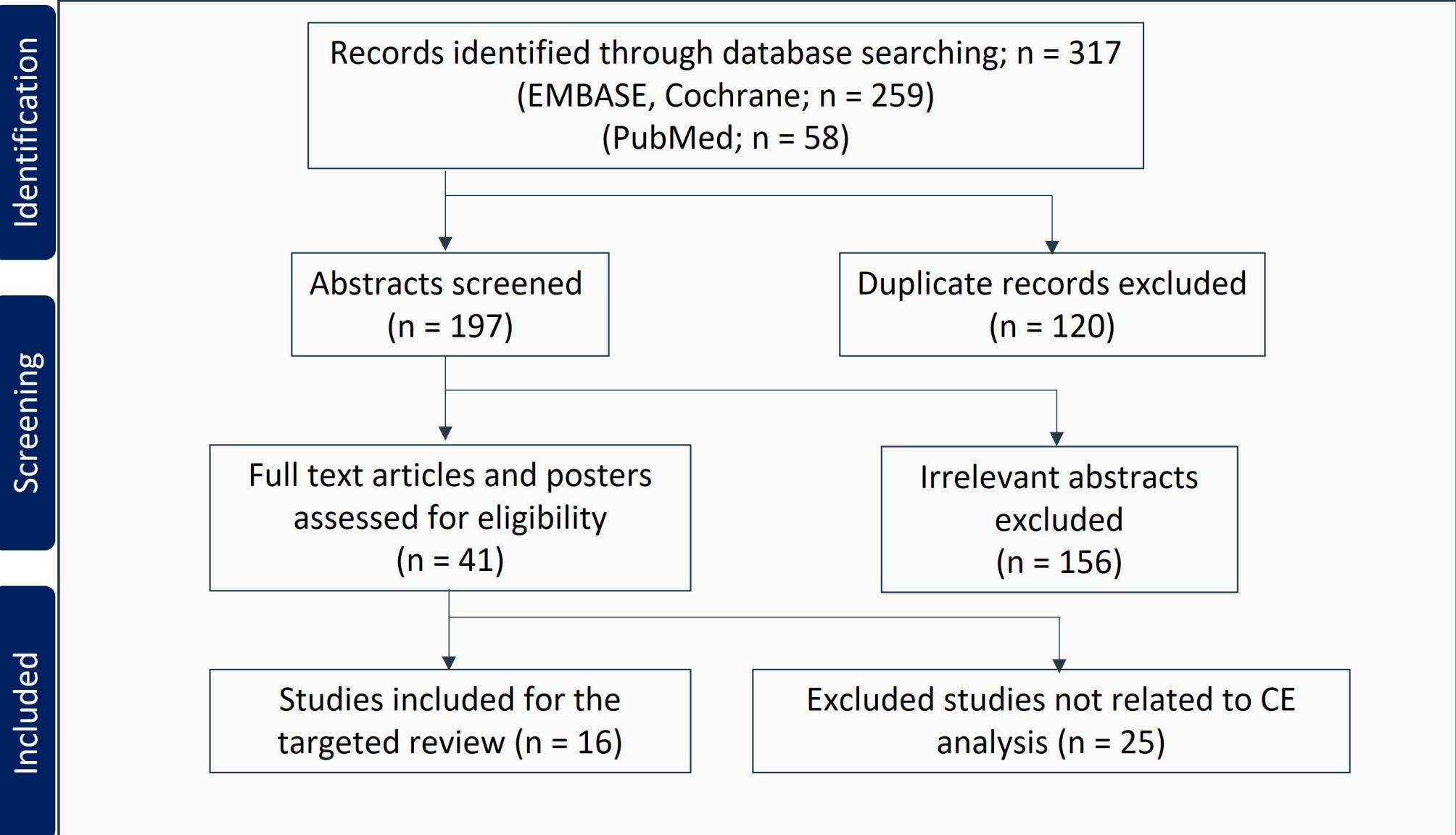
Methods

- Electronic databases such as PubMed, EMBASE, and Cochrane were used to perform a targeted literature search.
- The articles were screened against pre-defined eligibility criteria based on PICOS (Population, Intervention, Comparator, Outcomes, Study design), as in Table 1.
- Search was limited to English language, last conducted on 28 June 2022, with a 5-year and country filter.
- De-duplication was performed manually.
- The detailed search strategy is described in Figure 1.

Table 1: Screening of articles based on PICOS criteria	
Patient population	Previously treated and untreated mNSCLC patients (without driver mutations)
Intervention	ICIs (nivolumab, pembrolizumab, atezolizumab, durvalumab)
Comparator	SoC Chemotherapy (platinum/non-platinum/taxol-based)
Outcomes	LYs, QALYs, ICER, total cost
Study design	Cost-effectiveness analysis

ICER, Incremental cost-effectiveness ratio; ICI, Immune checkpoint inhibitor; LY, Life year; NSCLC, Non-small cell lung cancer; PICOS, Population, Intervention, Comparator, Outcomes, Study design; SoC: Standard of care; QALY, Quality-adjusted life years

Figure 1: Flow chart for identification of articles related to the targeted review of cost-effectiveness of ICIs in mNSCLC



CE, Cost-effectiveness; ICI, Immune checkpoint inhibitor; mNSCLC, Metastatic non-small cell lung cancer

Results

- Sixteen cost-effectiveness studies were identified, of which fifteen were from a healthcare payer perspective.
- First-line (1L) pembrolizumab monotherapy in previously untreated mNSCLC patients expressing PD-L1 TPS ≥50% resulted in QALY gains (range 0.74–1.34) versus SoC chemotherapy (n=4) (Table 2).

- Of all 4 countries, pembrolizumab monotherapy was not cost-effective in the UK (Table 2) due to a higher current willingness-to-pay (WTP) threshold.¹⁰

Table 2: Cost-effectiveness of 1L pembrolizumab versus SoC chemotherapy	
Country wise outcomes	Incremental gain
Switzerland¹	
LYs	1.69
QALYs	1.34
Costs	CHF 77,060
WTP threshold (CHF/QALY)	100,000
ICER (CHF/QALY)	57,402
France²	
LYs	0.93
QALYs	0.74
Costs	€ 37,064
WTP threshold (€/QALY)	170,000
ICER (€/QALY)	84,097
UK³	
QALYs	0.74
Costs	USD 83,000
WTP threshold (USD/QALY)	42,048
ICER (USD/QALY)	115,000
Switzerland⁴	
LYs	0.29
QALYs	0.83
WTP threshold (CHF/QALY)	100,000
Costs	CHF 56,585
WTP threshold (CHF/QALY)	100,000
ICER (CHF per QALY)	68,580

CHF, Swiss Franc; ICER, Incremental cost-effectiveness ratio; 1L, First-line; LY, Life year; QALY, Quality-adjusted life years; USD, United States dollars; UK, United Kingdom; WTP, Willingness-to-pay. References: 1) Bhaduri A et al. Swiss Medical Weekly, 2019; 2) Chouaid C et al. Lung Cancer, 2019; 3) Georgieva et al. Lung cancer, 2018; 4) Barbier MC et al. Eu J Health Econ, 2021

- Durvalumab consolidation following chemoradiotherapy for patients with unresectable mNSCLC and PD-L1 TPS ≥ 1% was also estimated to be cost-effective (n=3), with an increase in mean QALYs in Italy (2.73), Switzerland (1.18), and the UK (2.51) (Table 3).

Table 3: Cost-effectiveness of 1L durvalumab consolidation versus chemoradiotherapy	
Country wise outcomes	Incremental gain
Switzerland¹	
LYs	1
QALYs	0.76
Costs	CHF 67,239
WTP threshold (CHF/QALY)	100,000
ICER (CHF/QALY)	88,703
Italy²	
LYs	0.16
QALYs	0.24
Costs	€ 10,020
WTP threshold (€/QALY)	16,372
ICER (€/QALY)	42,322
UK³	
LYs	3.07
QALYs	2.51
Costs	£ 56,800
WTP threshold (£/QALY)	30,000
ICER (£/QALY)	22,665

CHF, Swiss Franc; ICER, Incremental cost-effectiveness ratio; 1L, First-line; LY, Life year; QALY, Quality-adjusted life years; UK, United Kingdom; WTP, Willingness-to-pay. References: 1) Panje CM et al. Ann of Onco, 2020; 2) Armeni P et al. Clin Ther, 2020; 3) Dunlop W et al. Pharmcoecon, 2022

- Among 1L treatments, pembrolizumab was more cost-effective versus nivolumab in Germany, but not in France (n=2, Table 4).

Table 4: Cost-effectiveness of pembrolizumab versus nivolumab	
Country wise outcomes	Incremental gain
Germany¹	
LYs	0.06
QALYs	0.08
Costs	€ 4,914
WTP threshold (€/QALY)	120,000
ICER (€/QALY)	81,567
France²	
LYs	0.06
QALYs	0.04
Costs	€ 5,582
WTP threshold (€/QALY)	120,000
ICER (€/QALY)	144,357

ICER, Incremental cost-effectiveness ratio; LY, Life year; QALY, Quality-adjusted life years; WTP, Willingness-to-pay. References: 1) Verma J et al. Cancer-Eco Evalu, 2020 (PCN36); 2) Verma J et al. Cancer-Eco Evalu, 2020 (PCN37)

- In previously treated mNSCLC patients, nivolumab monotherapy was shown to be cost-effective as compared to docetaxel in Sweden (n=1, Table 5).

Table 5: Cost-effectiveness of nivolumab versus docetaxel	
Country wise outcomes	Incremental gain
Sweden¹	
LYs	1.28
QALYs	0.94
Costs	SEK 535,333
WTP threshold (SEK/QALY)	750,000
ICER (SEK/QALY)	568,895

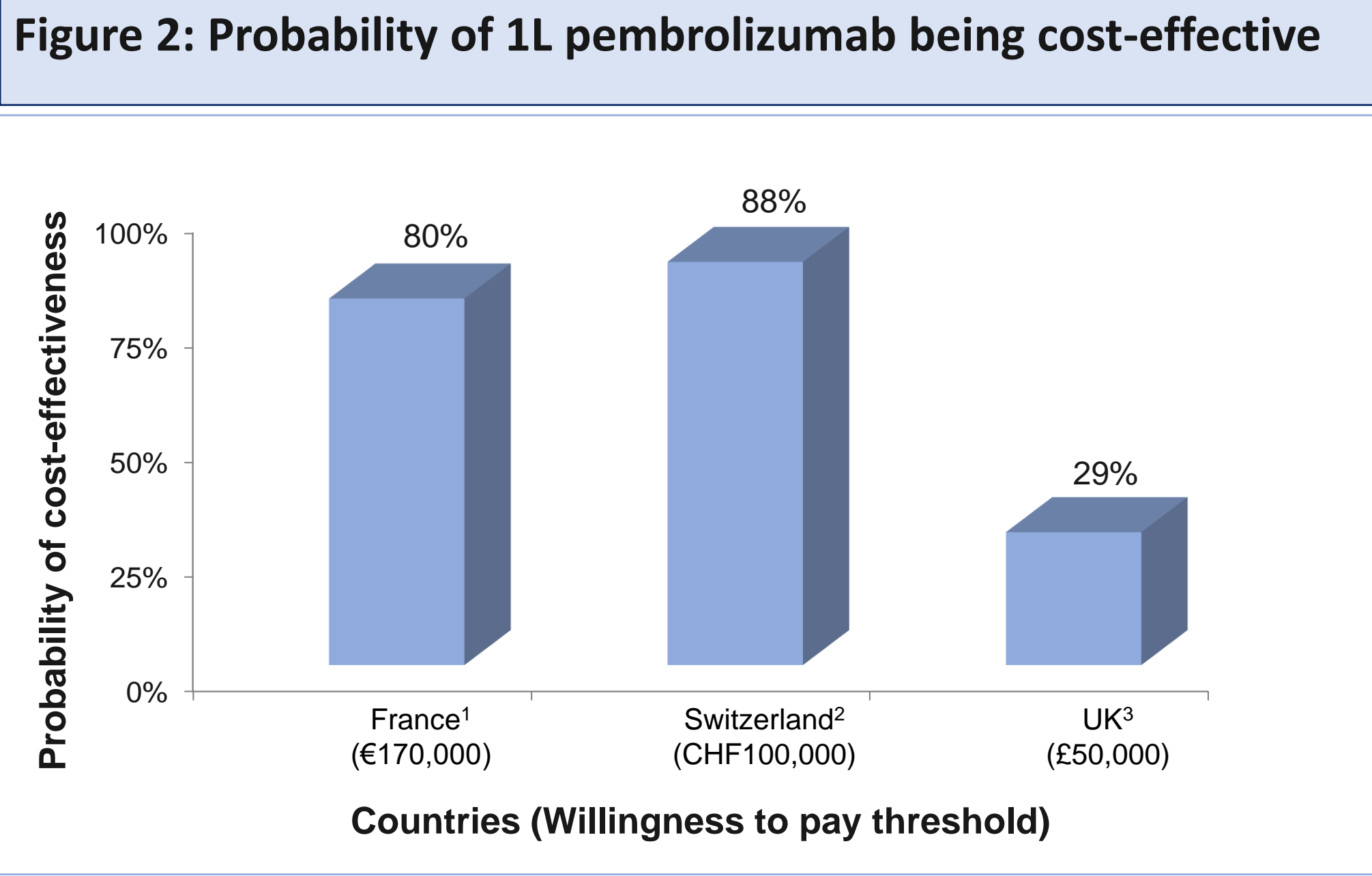
ICER, Incremental cost-effectiveness ratio; LY, Life year; QALY, Quality-adjusted life years; SEK, Swedish Krona; WTP, Willingness-to-pay. References: 1) Chaudhary et al. J Med Econ, 2021

- At second-line (2L), atezolizumab was more efficient but costlier than docetaxel in the treatment of mNSCLC in France (n=1, Table 6).

Table 6: Cost-effectiveness of 2L atezolizumab versus docetaxel	
Outcomes ¹	Incremental gain
QALYs	0.47
Costs	€ 49,429
WTP threshold (€/QALY)	150,000
ICER (€/QALY)	104,835

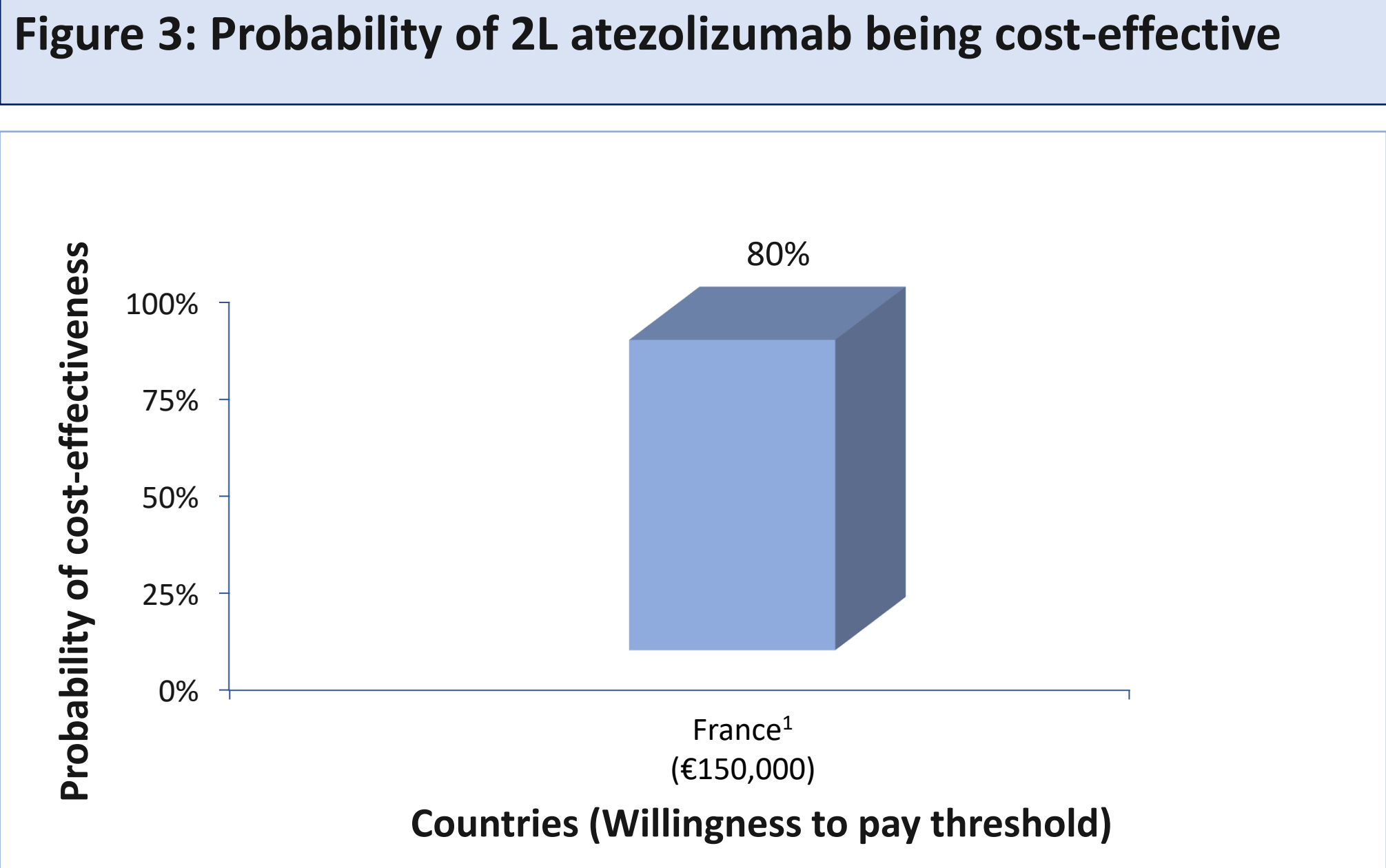
ICER, Incremental cost-effectiveness ratio; 2L, Second-line; QALY, Quality-adjusted life years; WTP, Willingness-to-pay. References: 1) Marine S et al. J Med Econ, 2020.

- At the specified WTP threshold of €170,000/QALY, CHF 100,000/QALY, and £50,000/QALY, the probability of 1L pembrolizumab being cost-effective was 80%, 88%, and 29% in France, Switzerland, and the UK , respectively (Figure 2).



CHF, Swiss Franc; 1L, First-line; UK, United Kingdom
References: 1) Chouaid C et al. Lung Cancer, 2019; 2) Bhaduri A et al. Swiss Medical Weekly, 2019; 3) Hu X et al. Lung Cancer, 2018.

- At a WTP threshold of €150,000/QALY, the probability of 2L atezolizumab being cost-effective was 80% in France (Figure 3).



2L, Second-line
References: 1) Marine S et al. J Med Econ, 2020.

Conclusion

- Our targeted review summarises the cost-effectiveness of immunotherapies in mNSCLC in selected EU nations.
- However, further research is needed to demonstrate how these pharmacoeconomic analyses can guide clinicians/policymakers in the timely adoption of these therapies to maximise patient benefit.

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